REMARKS

Status of the claims

Claims 1-7, 9-16 and 18 are cancelled. Claims 8 and 17 have been amended herein. Claims 8 and 17 have been amended to incorporate the subject matter of claim 13. No new matter has been added by this amendment.

Rejections under 35 U.S.C.§103

Claims 8, 10-13, 17 and 18 remain rejected under 35 U.S.C. §103 as being obvious over Kondo et al., Harada et al., and Shirakawa et al. For showing the state of the art at the time of the invention, the Examiner relies on Kuroki et al., Graham et al. and Crawford. The Examiner newly relies on Kuroki et al. and Crawford. The Examiner also newly relies on Trapani et al.

In response to Applicants' arguments of October 27, 2004 and January 5, 2005, the Examiner takes the position that, based on the teachings of the prior art, one skilled in the art would be able to understand and predict both the role of Fas in PBC or bile duct disappearance caused by an immune mechanism, and the use of a Fas antagonist to treat the disease states. The Examiner relies on the newly cited references of Kuroki et al., Trapani and Crawford et al. for the following asserted teachings. Kuroki et al. is asserted to teach that the initial injury in PBC is caused by the destruction of portal bile ducts and that Fas antigen is important in the death of biliary epithelial cells. Thus, Kuroki et al. is relied upon as an additional piece of evidence in support of the Examiner's assertion that the involvement of Fas in PBC was known in the art at the time of the invention. Trapini et al. is a general review article on the mechanisms of the induction of apoptosis by lymphocytes. The Examiner asserts that drug-induced hepatitis is clinically indistinguishable from viral and autoimmune hepatitis and Crawford is relied on by the Examiner in support of this assertion. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The instant invention has been limited to the very specific treatments of primary biliary cirrhosis or bile duct disappearance syndrome caused by an immunological mechanism by administering an anti-Fas ligand antibody, which inhibits Fas/Fas ligand binding. Thus, the instant invention is drawn to a specific immunotherapy. Success with an immunotherapy by

administering an antibody in 1998, i.e. at the time of the invention, was highly unpredictable such that there could be no expectation of success with the invention prior to actually conducting *in vivo* studies on an animal model. Thus, it was not possible to predict the success of the invention until the Applicants actually completed the studies conducted in Examples 3 and 5 of the specification.

Claims 8, 10-13, 17 and 18 remain rejected under 35 U.S.C. §103 as being obvious over Kondo et al., Harada et al., Shirakawa et al., Galle et al., Dienes et al. and Luo et al. With this rejection the Examiner also newly relies on Kuroki et al., Crawford and Tapani et al. Applicants traverse this rejection and withdrawal thereof is respectfully requested. The additional references that the Examiner relies upon fail to give any indication as to the likelihood of success with the present invention. As such, claims 8 and 17, as amended, are not obvious over Kondo et al., Harada et al., Shirakawa et al., Galle et al., Dienes et al. and Luo et al. Withdrawal of the rejection and allowance of claims 8 and 17 are respectfully requested.

In summary, even if the cited references collectively suggest the presently claimed invention (a point not conceded herein) the invention is not *prima facie* obvious because of a lack of a reasonable expectation of success (see MPEP § 2143.02).

In view of the above amendments and remarks, Applicant believes the pending application is in condition for allowance. Should the Examiner have any questions regarding the present application, she is requested to contact the undersigned.

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Respectfully submitted,

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